

## **REMARKS/ARGUMENTS**

Claims 1-11 are pending in the present application. With the present Amendment, claim 3 has been cancelled and claims 1, 8-9 and 11 have been amended. For at least the reasons that follow, Applicant submits that claims 1-2 and 4-11, as amended, are in condition for allowance.

### ***35 U.S.C. § 112 (Indefiniteness)***

Claims 1-11 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite because of parenthetical subject matter contained in independent claims 1 and 11. Claims 1 and 11 have been amended for purposes of clarification. Applicant respectfully submits that claims 1-2 and 4-11, as amended, are definite.

### ***35 U.S.C. § 112 (Enablement)***

Claims 1-11 stand rejected under 35 U.S.C. § 112, first paragraph, for the stated reason that the specification does not reasonably provide enablement for methods of “prophylaxis” within the full scope of the claims. In order to advance prosecution, claims 1, 8-9 and 11 have been amended to remove reference to “prophylaxis.” Claim 3 has been cancelled. In view of these amendments, Applicant respectfully requests that the rejection of claims 1-2 and 4-11 as lacking enablement be withdrawn.

**35 U.S.C. § 103(a) (Obviousness)**

Claims 1-11 stand rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 6,562,629 to Lin et al. Claim 3 has been cancelled. Applicants respectfully submit that claims 1-2 and 4-11, as amended, are patentable over Lin.

Contrary to the Office Action, Lin does not teach or suggest the use of balsalazide to treat irritable bowel syndrome (IBS). Nor does Lin provide a reasonable expectation of success in using balsalazide to treat IBS in a human. At best, Lin suggests that 5-amino salicylic acid (5ASA) compounds including balsalazide may be used to treat small intestinal bacterial overgrowth (SIBO) which may be a contributing factor to IBS.

The Office Action relies on col. 18 lines 4-21 of Lin, which states that 4 and 5 ASA compounds could be used to “at least partially eradicate the SIBO condition” (line 6). Balsalazide is listed in line 21 as one among many other aminosalicylate compounds that may be suitable. Nowhere in column 18 (or elsewhere in Lin), however, is the use of balsalazide referred to in the direct treatment of IBS.

Notably, IBS – a condition of the large intestine – is not the same thing as SIBO – a condition of the small intestine. Lin itself supports the distinction between the two conditions. For example, the Abstract differentiates between small intestinal bacterial overgrowth and IBS. Furthermore, in column 13, Lin

suggests that “small intestinal bacterial overgrowth (SIBO)” can be a contributing factor to a number of different conditions including MS, SLE, CD, ADHD, CFS as well as IBS. Linn does not state, however, that IBS is SIBO and in fact generally speaking when you have “small intestinal bowel overgrowth” there is an infection component and that infection usually carries inflammation (characteristics typically not associated with IBS). Hence, Lin does not in any way refer to the use of balsalazide to treat IBS but instead refers to the use of balsalazide to “partially eradicate the SIBO condition” which may be complicating IBS.

In further support of the above, it is noted that column 20, lines 45-50 of Lin teach the administration of an additional agent in order to treat IBS. Again, Lin discloses that the purpose of the treatment is to “at least partially eradicate[e] the bacterial overgrowth of the small intestine”. Given that Lin is directed to treatment of a different condition (SIBO), a person of ordinary skill in the art would not have found it obvious from Lin’s teachings to use balsalazide to treat IBS.

The non-obviousness of the presently claimed subject matter is supported by unexpected results. As noted above, Lin lists balsalazide as one among many other 4 and 5 ASA compounds that may be suitable for partially eradicating the SIBO condition (as opposed to IBS), but does not suggest that balsalazide offers any particular benefit over the other compounds in the list. As stated on pages 5 and 6 of the present specification, the inventor discovered that treatment of patients with

non infectious bowel disorders with 5ASA compounds such as mesalazine and olsalazine or with 4ASA compounds such as 4-aminosalicylic acid, whether alone or in combination with 5ASA compounds, whilst capable of suppressing symptoms in most patients with diarrhoea-predominant IBS symptoms may be even more effective when balsalazide is administered alone or in combination. From clinical experience, it has been found by the inventor that balsalazide is much more powerful at suppressing the symptoms of diarrhoea-predominant irritable bowel syndrome than the conventional 4ASA and 5ASA compounds. Balsalazide is better than mesalazine (5-ASA) in controlling and may inhibit even more powerfully the symptoms of diarrhoea-predominant IBS and associated conditions. This is unexpected. It was not expected that balsalazide would be capable of treating diarrhoea-predominant IBS as it is a very different molecule to the conventional 4ASA and 5ASA compounds. Balsalazide and its sodium salt is composed of a 5-amino salicylic acid joined to an unusually long chain, 4-amino benzoyl- $\beta$ -alanine (4-ABA). It is therefore a much larger molecule and does not belong to the same molecular shape as mesalazine or olsalazine. The inventor found that balsalazide can substantially inhibit the symptoms of diarrhoea in patients with diarrhoea-predominant IBS. It is thought that this is due to a large extent to the properties of the unique 'inactive carrier' side chain (4-ABA). It is noted that the side chain together with the 5-ASA potentiates inhibition of gas

production, cramping, fluid secretion, and mucus production. It appears the large side chain apart from the salicylate component is effective in treating diarrhoea.

***Conclusion***

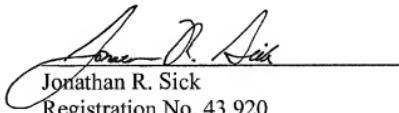
For the foregoing reasons, the Examiner is respectfully requested to prepare a Notice of Allowability allowing all the pending claims 1-2 and 4-11.

If the Examiner has any questions or the Applicant can be of any assistance, the Examiner is invited and encouraged to contact the Applicant at the number below.

It is to be noted that amendments to the pending claims set forth in the present Amendment are made solely for the purpose of advancing prosecution of the present application, and are not intended as an acquiescence to the propriety of the Examiner's rejections of the pending claims. To this end, Applicants reserve the right to pursue one or more claims of broader or similar scope prior to the amendments set forth herein in one or more continuing applications.

Please charge any required fees, or credit any overpayment, incurred in connection with this submission to Deposit Account No. 13-0017.

Respectfully submitted,



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